

Claims

We claim:

1. A pharmaceutical composition comprising an active agent having a lactone ring and a transition metal ion, wherein said ion is present at sufficient concentration to stabilize said lactone.
2. The composition of claim 1 wherein the pH of the preparation is between 6.0 and 8.0.
3. The composition of claim 1 wherein at least 40 mole % of the active agent is present in the ring-closed, lactone form at physiological pH.
4. The composition of claim 1 wherein at least 50 mole % of the active agent is present in the ring-closed, lactone form at physiological pH.
5. The composition of claim 1 wherein the active agent is camptothecin or a related analog.
6. The composition of claim 5 wherein the camptothecin is a water-soluble analog.
7. The composition of claim 6 wherein the water-soluble analog is selected from the group consisting of topotecan, irinotecan and lurtotecan.
8. The composition of claim 1 wherein the active agent and the metal are at a concentration of greater than 100 μM .
9. The composition of claim 1 wherein the transition metal complexes with the active agent through the oxygen coordination sites on the lactone ring.
10. The composition of claim 1 wherein said ion is of transition metal is selected from the group consisting of Cu, Zn and Co.

11. The composition of claim 10 wherein the transition metal is Cu.
12. The composition of claim 1 wherein the active agent and the transition metal ion are stably associated with one or more delivery vehicles.
13. The composition of claim 12 wherein the delivery vehicle is selected from the group consisting of lipid carriers, liposomes, lipid micelles, lipoprotein micelles, lipid-stabilized emulsions, cyclodextrins, polymer nanoparticles, polymer microparticles, block copolymer micelles, polymer-lipid hybrid systems and derivatized single chain polymers.
14. The composition of claim 13 wherein the delivery vehicle is a liposome.
15. The composition of claim 14 wherein the liposome is a large unilamellar liposome.
16. The composition of claim 12 wherein the delivery vehicle is a liposome and the transition metal ion is Cu + 2.
17. The composition of claim 12 wherein the active agent is a camptothecin.
18. The composition of claim 17 wherein the camptothecin is a water-soluble analog selected from the group consisting of lurtotecan, topotecan and irinotecan.
19. The composition of claim 13 wherein the delivery vehicle is a polymer nanoparticle.
20. The composition of claim 19 wherein one or more polymers making up the nanoparticle are complexed with a transition metal ion.
21. The composition of claim 20 wherein the nanoparticle comprises a stabilizing lipid.